24. (Amended) The method of claim 23 wherein said morphogen is selected form the group consisting of: OP-1 OP-2, BMP-2, BMP-4, BMP-5, and BMP-6.

B^3 cont.

25 (Amended) The method of claim 1 ~~or 3~~ wherein said morphogenic protein is a morphogenically active amino acid sequence variant of a morphogen comprising an amino acid sequence having at least 70% homology within the C-terminal 102-106 amino acids, including the conserved seven cysteine domain, of human OP-1.

REMARKS

In the Office Action of October 23, 2001, claims 1-5, 12-14, 20 and 23-28 were rejected under 35 U.S.C. 102(b) as being anticipated by Rueger et al., WO 94/03200. Claims 8-11, 15-19, 21 and 22 have also been rejected under 35 U.S.C. 103(a) as obvious over Rueger et al. These grounds of rejection are respectfully traversed.

Rueger et al. is directed to the use of morphogens for maintaining neural pathways in mammals and enhancing the survival of neurons at risk of dying. The Examiner contends that Rueger et al. teaches animal models in which lesions are intentionally induced, such as by crushing the optic nerve or transecting the sciatic nerve. The Examiner also states that Rueger et al. discloses systemic administration of the morophogen, and genetic or environmental damage. Finally, the Examiner states that the reference teaches the administration of morphogens at different time intervals.

The claims of this application specify that the morphogen is administered to a site distal or remote from the site of a local defect in the mammal. A local defect is one to which progenitor cells are accessible. See page 5 of the specification. As stated in more detail in the specification, mesenchymal progenitor cells typically become available to a defect locus 6 to 24 hours post trauma, as part of the inflammatory response triggered by the initial trauma. The claims have now been amended in order to incorporate this definition.

Although the Examiner points to pages 90 to 93 as disclosing applicants' claimed invention, there is no indication from this disclosure that the reference meets applicants' claims.

The morphogen in the reference is applied directly to the optic nerve, not at a point distal from the optic nerve. Moreover, there is no evidence that the site of local permissive defect, i.e. injury to the optic nerve, is a site to which progenitor cells are readily available or accessible.

The method of this invention is intended to be used for **candidate** morphogens which have not been previously evaluated for morphogenic activity or optimal dosage. The morphogens of the reference, according to the Examiner's interpretation, have been evaluated for these properties. Accordingly, the reference would not apply to such morphogens, since these references would not be **candidate** morphogens. See, also, claims 23-25 which cover variants of morphogenic compounds which have not been previously characterized or evaluated for activity or dosing. Claims 23-25 would not be anticipated or rendered obvious by the Rueger et al. reference.

Claims 1-5 and 8-28 stand rejected under 35 U.S.C. 103(a) as obvious over the Wang et al. reference. This ground of rejection is also traversed.

Wang et al. relate to methods for inducing the growth of neural cells, and repairing neural defects in a mammal, by administering a bone morphogenic protein. The Examiner states that Wang et al. teaches the evaluation of BMP-2, as well as intravenous administration. However, the Examiner acknowledges that the reference fails to disclose a method of evaluating morphogens.

The Wang et al. reference to the use of known BMP morphogens for growing and repairing neural cells. The candidate morphogens of the present invention would not encompass these cells for the reasons presented above in connection with the discussion of the Rueger et al. reference. Moreover, the reference does not teach or suggest a method for evaluating the activity or optimal dosage of the morphogen, and the reference fails to teach or suggest the creation of a local permissive defect site in a mammal to which progenitor cells are readily accessible or available as required by the present claims. Accordingly, the Wang et al. reference is even further removed from the present claims than the Rueger et al. reference.

In view of the foregoing remarks and consideration, reconsideration and withdrawal of the rejects is urged. Entry of this amendment is proper at this time since it does not raise any new issues, nor does it require any further search or consideration on the part of the Examiner.

Accordingly, this application is believed to be in proper condition for allowance, and such action at an early date is solicited.

Respectfully submitted,

by William Gosz

William G. Gosz
Reg. No. 27,787
Ropes & Gray
One International Place
Boston, MA
Attorneys for Applicant(s)
Tel. No. (617) 951-7000

DATE: 2/28/02

iManage 8665829

MARKED-UP CLAIMS

1. (Twice Amended) A method for evaluating the morphogenic activity of a candidate morphogenic protein or analog thereof, the method comprising the steps of:

(a) creating, for purposes of the evaluation, a local [permissive] defect site in a mammal accessible to progenitor cells,

(b) administering said candidate morphogenic protein or analog systemically to said mammal at a site distal from the local permissive defect site,

(c) measuring the ability of the candidate protein or analog to induce new tissue formation at said defect site, and

(d) comparing the ability of said candidate with the ability of a control to perform the same function.

3. (Twice Amended) A method for evaluating the optimal dosage of a candidate morphogenic protein or analog thereof, the method comprising the steps of:

(a) creating, for purposes of the evaluation, a local [permissive] defect site in a mammal accessible to progenitor cells,

(b) administering said candidate morphogenic protein or analog systemically to said mammal at a site distal from the local permissive defect site,

(c) measuring the ability of the candidate protein or analog to induce new tissue formation at said defect site, and

(d) comparing the ability of said candidate with the ability of a control to perform the same function.

23. (Amended) The method of claim 1 or claim 3 wherein said morphogenic protein is a morphogenically active amino acid sequence variant of a morphogen selected from the group consisting of: OP1, OP2, OP3, BMP2, BMP3, BMP4, BMP5, BMP6, BMP9, BMP-10, BMP-11, BMP-12, BMP-15, BMP-3b, DPP, Vgl, Vgr, 60A protein, GDF-1,. GDF-3, GDF-5, GDF-6,

GDF-7, GDF-8, GDF-9, GDF-10, and GDF-11 [and morphogenically active amino acid sequence variants thereof].

24. (Amended) The method of claim 23 [claim 1 or 3] wherein said [morphogenic protein] morphogen is selected form the group consisting of: OP-1 OP-2, BMP-2, BMP-4, BMP-5, and BMP-6 [and morphogenically active amino acid sequence variants thereof].

25 (Amended) The method of claim 1 or 3 wherein said morphogenic protein is a [morphogen, said] morphogenically active amino acid sequence variant of a morphogen comprising an amino acid sequence having at least 70% homology within the C-terminal 102-106 amino acids, including the conserved seven cysteine domain, of human OP-1.